REMARKS

Claims 94-164 were pending in the application. Claims 112, 114-120, 127-156, and 159-164 have been cancelled herein without prejudice to their presentation in another application as being drawn to a non-elected invention. In addition, claims 95, 96, 104, 106, 107, 113, 121, 124, and 157 have been canceled without prejudice to their presentation in another application. Claims 94, 105, 123, 125, 126, and 158 have been amended herein. Upon entry of the present amendment, claims 94, 97-103, 105, 108-111, 122, 123, 125, 126, and 158 will be pending.

I. The Claimed Invention Is Novel

Claims 94-98, 100-102, 104-111, 113, 121, and 123-125 are rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Agrawal et al. (WO 94/01550; hereinafter the "Agrawal reference"). The Office Action asserts that the Agrawal reference discloses "self-stabilized oligonucleotides that are double stranded" (Office Action, page 3). Claims 95, 96, 104, 106, 107, 113, 121, and 124 have been canceled herein without prejudice to their presentation in another application. Applicant respectfully traverses the rejection as it is applied against the remaining claims and requests reconsideration in view of the amended claims.

Applicant has amended claims 94, 105, 123, and 125 to recite that the first and second strands are not covalently linked, support for which can be found at, for example, pages 92-93 of the specification. For example, Table 1 at page 93 of Applicant's specification clearly depicts double-stranded RNA compounds comprising two strands that are not covalently linked.

In contrast, the Agrawal reference reports self-stabilized antisense oligonucleotides having two regions: a target hybridizing region and a self-complementary region. The self-complementary region:

> contains oligonucleotide sequences that are complementary to other oligonucleotide sequences within the oligonucleotide. These other oligonucleotide sequences may be within the target hybridizing region or within the self-complementary region, or they may span both regions. The complementary sequences form base pairs, resulting in the formation of a hairpin structure, as shown in Figure 1, or a hammer-like structure, as shown in Figure 2.

(the Agrawal reference, page 15). The Agrawal reference does not teach or even suggest a

double-stranded RNA comprising first and second strands wherein the strands are not covalently linked, let alone methods of using such a compound.

In view of the foregoing, the Agrawal reference does not teach or suggest Applicant's claimed invention. Accordingly, Applicant respectfully requests that the rejection under 35 U.S.C. §102(b) be withdrawn.

II. The Claimed Invention Is Not Obvious

Claims 157 and 158 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over the combination of the Agrawal reference in view of Hunziker et al., *Nucleic Acid Analogues: Synthesis and Properties* in *Modern Synthetic Methods*, 1995, Ernst and Leumann, Eds., pp. 331-417 (hereinafter, the "Hunziker reference"). The Office Action asserts that the Hunziker reference is used because of its reporting of peptide nucleic acid modifications. Claim 157 has been canceled herein without prejudice to its presentation in another application. Applicant traverses the rejection as it is applied to claim 158 and respectfully requests reconsideration because even if combined, the cited references do not produce the claimed invention.

Applicant has amended claim 158 to recite that the first and second strands are not covalently linked. As stated above, the Agrawal reference does not teach or even suggest a double-stranded RNA comprising first and second strands wherein the strands are not covalently linked, let alone methods of using such a compound. Further, the Hunziker reference does not cure the deficiency of the Agrawal reference. The combination of the Agrawal reference and Huziker reference does not teach or suggest Applicant's claimed invention. Accordingly, Applicant respectfully requests that the rejection under 35 U.S.C. §103(a) be withdrawn.

III. The Claimed Invention Is Supported by Ample Written Description

Claims 94-103, 105-111, 123, 125, 126, 157, and 158 are rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. Claims

95, 96, 106, 107, and 157 have been canceled without prejudice to their presentation in another application. Applicant traverses the rejection with respect to the remaining rejected claims and respectfully requests reconsideration because the specification provides ample written description supporting the claimed inventions.

The requirements of §112, first paragraph, are met so long as: (1) the invention is described in the specification as broadly as it is claimed; and (2) the information provided in the specification is sufficient for persons of ordinary skill in the art having the specification before them to make and use the invention. *In re Marzocchi*, 169 U.S.P.Q. 367 (C.C.P.A. 1971). Indeed, the "function of the description required [under 35 U.S.C. §112, first paragraph,] is to ensure that the inventor had possession as of the filing date of the application relied on, of the specific subject matter claimed by him." *In re Edwards*, 196 U.S.P.Q. 465, 467 (C.C.P.A. 1978). The specification provides sufficient written description support for the claimed embodiments.

The Office Action asserts that the rejected claims are drawn to methods of modifying a target RNA, activating a nuclease within a cell, or modulating the levels of a target RNA via the contacting of a cell with a double stranded RNA that contains a modification. The specification amply supports such embodiments. For example, Applicant teaches at page 30, lines 10-34 of the specification that the phrase "target RNA" shall mean **any** RNA that can hybridize with a complementary nucleic acid-like compound (a first oligonucleotide, for example). Applicant further teaches that the term "complementary" refers to precise pairing or sequence complementarity **between a first and a second nucleic acid-like oligomers containing nucleoside subunits**. Thus, the RNA target that hybridizes with a complementary nucleic acid-like compound can be a second nucleic acid-like oligomer. Applicant further teaches that the term "complementary" is used to indicate a sufficient degree of complementarity such that stable and specific binding occurs between a compound of the invention (a first oligomer or oligonucleotide, for example) and a target RNA molecule (a second oligomer or oligonucleotide, for example). Thus, the modified oligonucleotides (such as the gapmers, for example) described in the specification are not limited to forming duplexes with mRNA targets. Rather, Applicant's specification teaches forming a duplex between these oligonucleotides and other oligomeric

compounds. Thus, the specification clearly describes duplexes formed from a first oligonucleotide and a second oligonucleotide.

The Office Action also asserts that there is no written description support in the specification for recitation of "cytoplasm of the cell" in claim 101, "nucleus of the cell" in claim 102, and "mitochondria of the cell" in claim 103. Although Applicant submits that the specification amply supports such claimed embodiments, solely to advance prosecution of the present application, claims 101-13 have been cancelled.

The Office Action also asserts that there is no support for recitation of "at least one peptide nucleic acid" in claim 158. The Office Action asserts that the specification supports only a plural number of peptide nucleic acid segments. Originally filed claim 50, however, provides written description support of a compound that has a peptide nucleic acid subunit as the surrogate nucleoside subunit. Thus, the specification provides sufficient written description support wherein a compound may have a single peptide nucleic acid.

The Office Action also asserts that there is no support for recitation of "a compound" in claim 158. The Office Action asserts that the only support in the specification "oligomeric compounds." Solely to advance prosecution, Applicant has amended claim 158 to recite "oligomeric compound."

In view of the foregoing, Applicant respectfully requests that the rejection under 35 U.S.C. §112, first paragraph, as allegedly failing to provide sufficient written description be withdrawn.

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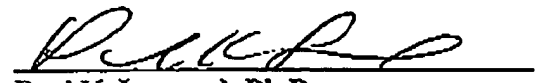
IV. Conclusion

In view of the foregoing, Applicant respectfully submits that the claims are in condition for allowance. An early notice of the same is earnestly solicited. The Examiner is invited to contact Applicant's undersigned representative at (215) 665-6914 if there are any questions regarding Applicant's claimed invention.

Respectfully submitted,



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